

AMENDMENTS TO THE SPECIFICATION

At page 54, line 19 (after the chemical structure), please replace the paragraph with the following new paragraph:

Oxytocin analogue (13) (SEQ ID NO: 1)

At page 55, line 7 – page 56, line 25, please replace the paragraph with the following new paragraph:

Oxytocin analogue (13) with the sequence (one letter code) Acetyl-CYIQNCPLGK(COCH₂CH₂CONHNH₂)-NH₂ (SEQ ID NO: 1), was synthesised manually using Fmoc/tBu protection strategy on TGR resin (0.25 g, 0.05 mmol, substitution: 0.2 mmol/g). Coupling of the Fmoc amino acids was accomplished with an HBTU/HOBt method utilising dimethylformamide as the solvent, using 3 equivalents of amino acid and coupling reagents with respect to the loading of the resin. The Fmoc group was removed by a 15 min treatment with 20% piperidine in dimethylformamide. The C-terminal lysine residue was introduced with Dde side chain protection, to allow orthogonal deprotection at a later stage in the synthesis. After Fmoc deprotection of the final residue, the N-terminus was acetylated using acetic anhydride (48 µL, 0.5 mmol) and diisopropylethylamine (43 µL, 0.25 mmol) in dimethylformamide for 2 hours and the Dde protection of the lysine side chain removed with 2% hydrazine in dimethylformamide for 15 mins. The free amine of the lysine side chain was extended by reaction with succinic anhydride (50 mg, 0.5 mmol) and diisopropylethylamine (43 µL, 0.25 mmol) in dimethylformamide for 2 hours and then hydrazine, coupled as a 10% solution in dimethylformamide using HBTU/HOBt (in excess) for 3 hours. Final cleavage of the peptide from the resin was performed with 92.5% trifluoroacetic acid/2.5% triisopropylsilane/2.5% water/2.5% ethanedithiol (40 mL/g resin) for 75 mins. The resin was removed by filtration and the filtrate was concentrated by sparging with nitrogen. The crude product was precipitated and washed with cold methyl tert-butyl ether (3 x 50 mL), before being re-dissolved in 50% (aq.) acetonitrile and lyophilised. The peptide was re-dissolved in ammonium bicarbonate (0.1 M, pH

8) to a concentration of 100 μ M and oxidised using hydrogen peroxide (1.5 eq) for 45 mins. The reaction was monitored by LC-ESI-MS and with Ellman's reagent and finally quenched with 10% (aq) acetic acid (in excess). The mixture was lyophilised once more and then purified by semi-preparative RP-HPLC. Yield: 24 mg, 0.019 mmol, 37%. ESI-MS m/z : 1291.3 (calc. for $M+H^+$ 1291.5). HPLC retention time: 3.44 mins.

At page 64, line 12 – page 65, line 2, please replace the paragraph with the following new paragraph:

The neurohypophysial hormone oxytocin, is a disulfide constrained nonapeptide (cyclo-[CYIQNC]PLG) (SEQ ID NO: 2), and was chosen as a model epitope with which to carry out conjugation and immunisation studies. Typically, the conjugation reactions between BSA-linker constructs (20-22) and epitope (13) were performed in an aqueous buffer/dimethyl sulfoxide medium at pH4-4.5. Loading reactions were complete after approximately 18 hours, using 2-3 equivalents of the oxytocin analogue hydrazide (13) with respect to the number of moles of aldehyde accessible for conjugation. Initially, only conjugates BSA-TML85-epitope13 (24) and BSA-BAL85-epitope13 (26) were adequately prepared since the poor solubility of the BSA-Tfa85 (21) construct hampered any synthetic efforts to produce the conjugate BSA-Tfa85-epitope13 (25). Upon dialysis into phosphate buffer (pH 7.4), however, the conjugate obtained from BSA-BAL85-epitope13 (26), precipitated and aggregated becoming very poorly soluble. In contrast, the conjugate BSA-TML85-epitope13 (24) remained relatively soluble with only a slight precipitate seen in the solution. In order to proceed with immunisation studies, a soluble conjugate based around BAL linker (17) was required and such a conjugate, BSA-BAL55-epitope13 (27), was obtained with a reduced surface loading of approximately 55%, through BSA-BAL55 (23). Solubility studies showed that the BSA-TML85-epitope13 (24) and BSA-BAL55-epitope (27) conjugates had good solubility at pH 6 and pH 7.4 of around 0.5 — 1 mg/mL (Figures 5 and 6).

In the specification, after the last page thereof, please insert the enclosed Sequence Listing, renumbering pages if required. A computer readable form of the sequence listing is also enclosed.